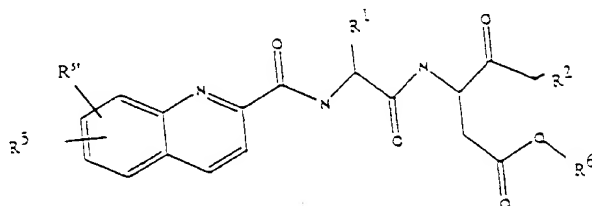


We Claim:

1. A compound of the structure:



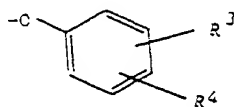
wherein in Structure I

R<sup>1</sup> is selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH-(R<sup>1</sup>)-(C=O)- will produce a natural amino acid structure or an unnatural amino acid structure, and;

the carbon adjacent to R<sup>1</sup> group is in the D or L configuration;

R<sup>2</sup> is selected from the group consisting of

- F; and

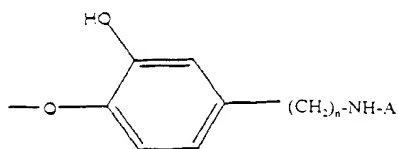


wherein R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino;

and R<sup>5</sup> and R<sup>6</sup> are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and together form a cyclic structure or a heterocyclic structure; and

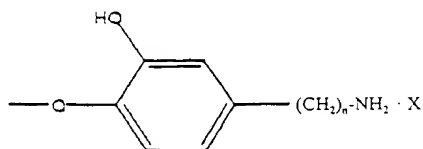
R<sup>6</sup> is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

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wherein A is a covalently bonded amine protecting group, and n is 1-4;

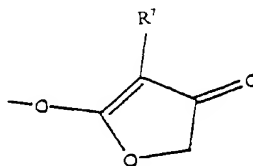
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wherein X is a pharmaceutically acceptable salt, and n is 1-4; or

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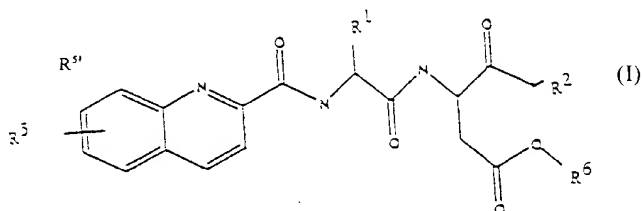
;

25

wherein  $R^7$  is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl.

2. A pharmaceutical composition for use as a protease inhibitor, which composition comprises

(a) a compound of the structure:



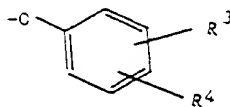
wherein in Structure I

R<sup>1</sup> is selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group -N-CH(R<sup>1</sup>)-(C=O)- will produce a natural amino acid structure or an unnatural amino acid structure, and;

the carbon adjacent to R<sup>1</sup> group is in the D or L configuration;

R<sup>2</sup> is selected from the group consisting of

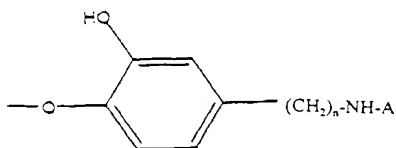
- F; and



25 wherein R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino;

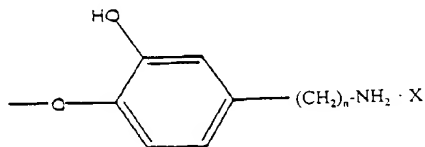
and R<sup>5</sup> and R<sup>5'</sup> are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino, and together can form a cyclic ring structure in a heterocyclic ring structure; and

30 R<sup>6</sup> is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;



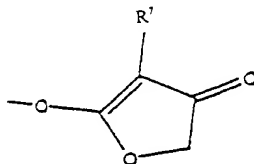
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wherein A is a covalently bonded amine protecting group, and n is 1-4;



10

where X is the pharmaceutically accepted salt, and n is 1-4;



15

wherein R<sup>7</sup> is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the pharmaceutically acceptable acid or base salts thereof, and  
(b) a pharmaceutically acceptable excipient.

20

3. The composition of Claim 2 wherein in the structure:

R<sup>1</sup> is selected from isopropyl or isobutyl;

R<sup>2</sup> is F; and R<sup>5</sup> is hydrogen.

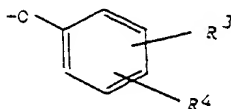
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4. The pharmaceutical composition of Claim 2 wherein in the structure:

R<sup>1</sup> is selected from isopropyl or isobutyl;

R<sup>2</sup> is

30



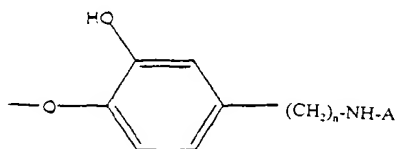
wherein  $R^3$  and  $R^4$  are each fluoro; and  $R^5$  is hydrogen.

5

5. The composition of Claim 4 wherein in the structure,  $R^3$  and  $R^4$  in the 2 and 6 positions of the phenyl ring.

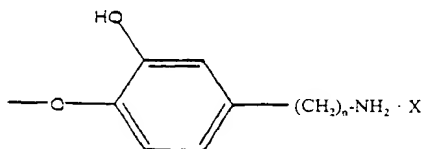
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6. The composition of Claim 5 wherein  $R^2$  is



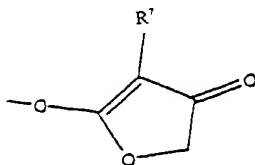
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7. The composition of Claim 5 wherein  $R^2$  is



20

8. The composition of Claim 5 wherein  $R^2$  is

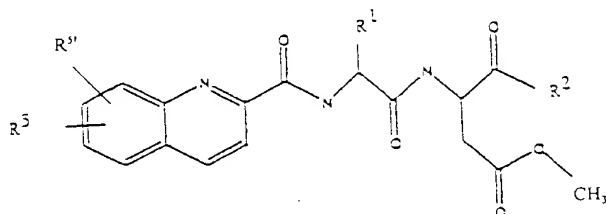


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9. A pharmaceutical composition for use as a protease inhibitor, which composition comprises,

(a) a compound of the structure:

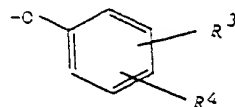


wherein

$R^1$  is selected from the group consisting of methyl, ethyl, isopropyl, and iso-butyl;

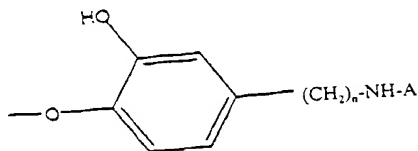
$R^2$  is selected from the group consisting of:

-F or

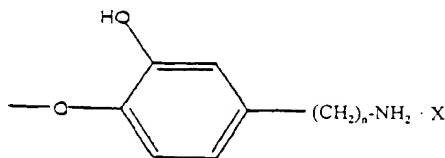


wherein  $R^3$  and  $R^4$  are each independently selected from the group consisting of hydrogen, alkyl having 1 to 10 carbon atoms, fluoro, chloro and amino;

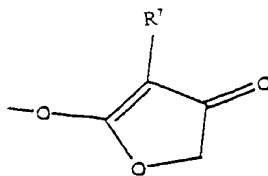
and  $R^5$  and  $R^{51}$  are each selected from the group consisting of hydrogen having 1 to 10 carbon atoms, alkyl having 1 to 10 carbon atoms, alkoxy having 1 to 10 carbon atoms, fluoro, and chloro;



wherein A is a covalently bonded amine protecting group, and n is 1-4;

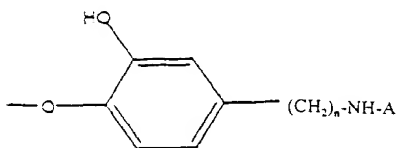


wherein X is a pharmaceutically acceptable salt and n is 1-4;

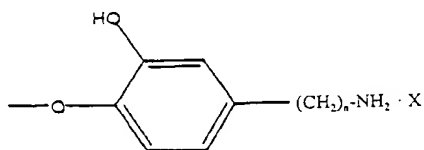


10 wherein R<sup>7</sup> is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl.

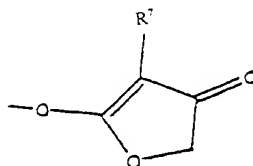
10. The composition of Claim 9 wherein R<sup>2</sup> is



20 11. The composition of Claim 9 wherein R<sup>2</sup> is

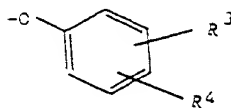


12. The composition of Claim 9 wherein R<sup>2</sup> is



13. The pharmaceutical composition of Claim 9, wherein in the structure:  
 $R^1$  is selected from isopropyl or iso-butyl;  
 $R^2$  is -F; and  
 $R^5$  is hydrogen.

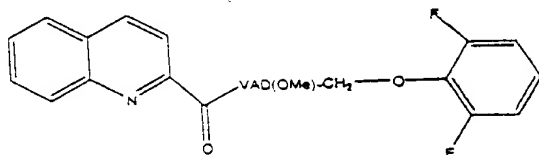
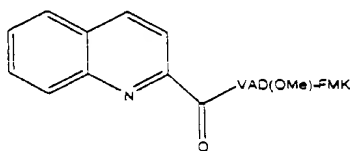
14. The pharmaceutical composition of Claim 9 wherein, in the structure  
 $R^1$  is selected from isopropyl or isobutyl;  
 $R^2$  is



wherein  $R^3$  and  $R^4$  are each fluoro; and  $R^5$  is hydrogen.

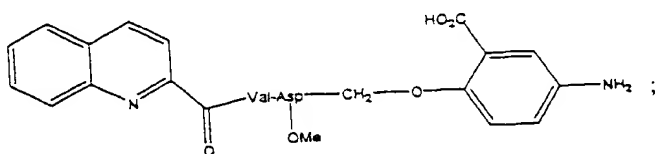
15. The pharmaceutical composition of Claim 9 wherein in the structure, groups  
 $R^3$  and  $R^4$  are in the 2 and 6 positions of the phenyl ring.

16. A pharmaceutical composition for use as an inhibitor to caspase or a caspase-like enzyme, which composition comprises  
 (a) a compound selected from the group consisting of:

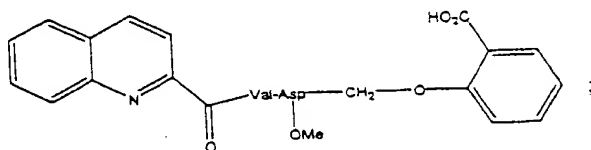




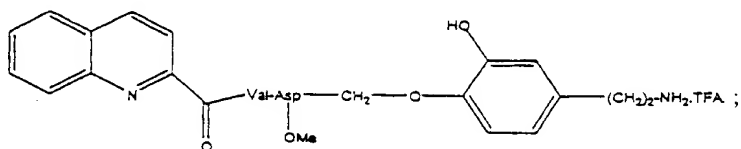
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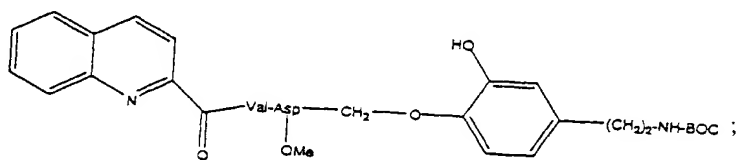
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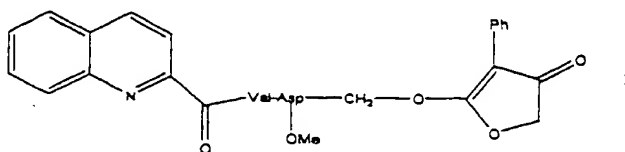


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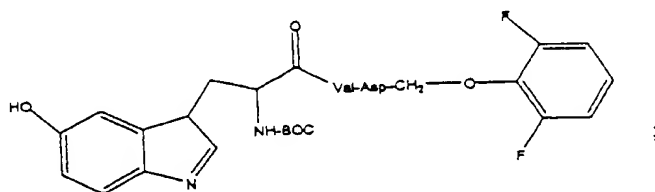


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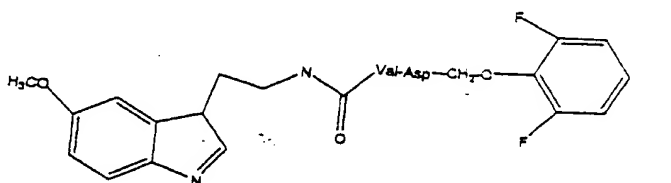


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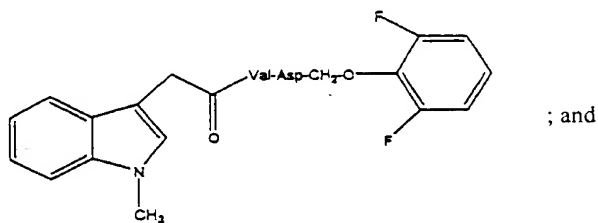
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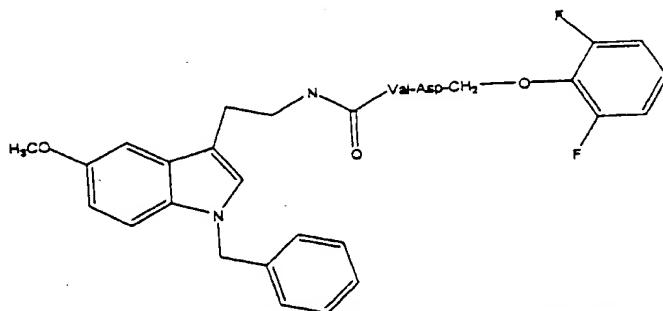


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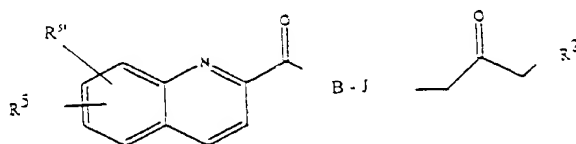


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(b) a pharmaceutically acceptable excipient.

17. A compound of the structure:



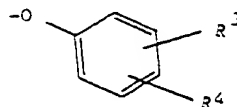
wherein

B and J are each selected from the group consisting of a natural amino acid structure or an unnatural amino acid structure, and;

the amino acid in the D or L configuration;

R<sup>2</sup> is selected from the group consisting of

- F and

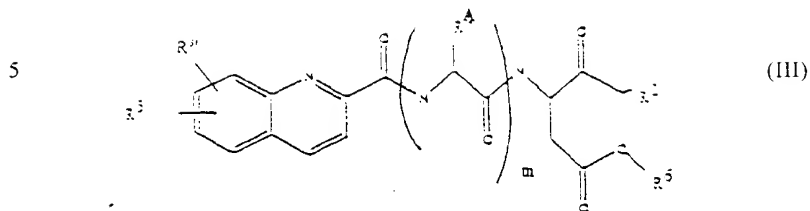


wherein R<sup>3</sup> and R<sup>4</sup> are each selected from the group consisting of hydrogen alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino; and

R<sup>5</sup> is selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkoxy, alkyl carbonyl, aryl carbonyl, and amino.

18. The compound of Claim 17 wherein groups B and J are both glycine and R<sup>2</sup> is fluoro and R<sup>5</sup> is hydrogen.

19. A compound selected of the structure:



10 wherein in Structure III:

m is 1, 2 or 3, creating 1, 2 or 3 amino acid linkages, such that

when m = 1,  $R^A = R^1$ ,

when m = 2,  $R^A$  is  $R^1$  and  $R^{1B}$  in the separate amino acids and

when m = 3,  $R^A$  is  $R^1$ ,  $R^{1B}$  and  $R^{1C}$  wherein  $R^1$ ,  $R^{1B}$  and  $R^{1C}$  in the separate amino acids

15 which amino acids are the same or different amino acid when  $R^1$ ,  $R^{1B}$  and  $R^{1C}$  are independently selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group  $-N-CH(R^1)-(C=O)-$ ;  $N-CH(R^1)-(C=O)-NH-CH(R^{1B})-(C=O)-$ ; or  $NCH(R^1)(C=O)-NH-CH(R^{1B})(C=O)-NHCH(R^{1C})(C=O)-$  produces natural amino acid structures or an unnatural amino acid structures, and;

20 the carbon adjacent to  $R^1$  group is in the D or L configuration;

$R^2$  is selected from the group consisting of:

- F; and

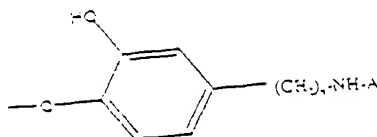


wherein  $R^3$  and  $R^4$  are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino;

30 and  $R^5$  and  $R^5$  are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and together form a cyclic ring structure or a heterocyclic ring structure; and

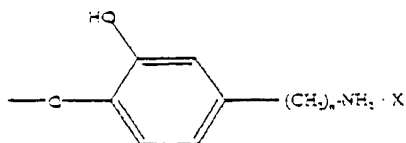
$R^6$  is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;

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wherein A is a covalently bonded amine protecting group, and  
n is 1-4, preferably 2;

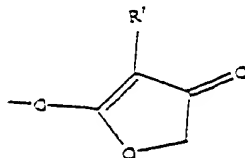
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where X is the pharmaceutically accepted salt, and  
n is 1-4, preferably 2; and

20



wherein  $R^7$  is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the pharmaceutically acceptable acid or base salts thereof.

25

20. The compound of Claim 19 wherein  $m = 2$ ,  $R^1$  and  $R^{1B}$  are each independently selected from methyl, ethyl, isopropyl and t-butyl.

21. The compound of Claim 19 wherein  $m = 3$ ,  $R^1$ ,  $R^{1B}$  and  $R^{1C}$  are each independently selected from methyl, ethyl, isopropyl and t-butyl.

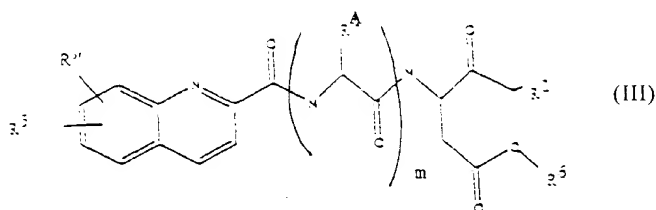
22. The compound of Claim 20 wherein  $R^2$  is F or 2,6-difluorophenoxy,  $R^5$  and  $R^5$  are each hydrogen and  $R^6$  is methyl.

30

23. The compound of Claim 21 wherein  $R^2$  is F or 2,6-difluorophenoxy,  $R^5$  and  $R^5$  are each hydrogen and  $R^6$  is methyl.

24. A pharmaceutical composition for use as a protease inhibitor having a

compound selected from the structure:



10 wherein in Structure III:

m is 1, 2 or 3, creating 1, 2 or 3 amino acid linkages, such that

when m = 1,  $R^A = R^1$ ,

when m = 2,  $R^A$  is  $R^1$  and  $R^{1B}$  in the separate amino acids and

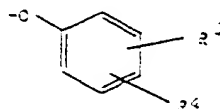
when m = 3,  $R^A$  is  $R^1$ ,  $R^{1B}$  and  $R^{1C}$  wherein  $R^1$ ,  $R^{1B}$  and  $R^{1C}$  in the separate amino acids

15 which amino acids are the same or different amino acid when  $R^1$ ,  $R^{1B}$  and  $R^{1C}$  are independently selected from the group consisting of alkyl, substituted alkyl, aryl, and substituted aryl which group  $-N-CH(R^1)-(C=O)-$ ;  $N-CH(R^1)-(C=O)-NH-CH(R^{1B})-(C=O)$ ; or  $NCH(R^1)(C=O)-NH-CH(R^{1B})(C=O)-NHCH(R^{1C})(C=O)-$  produces natural amino acid structures or an unnatural amino acid structures, and;

20 the carbon adjacent to  $R^1$  group is in the D or L configuration;

$R^2$  is selected from the group consisting of:

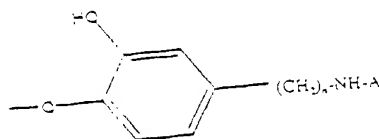
- F; and



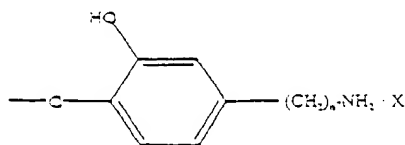
wherein  $R^3$  and  $R^4$  are each independently selected from the group consisting of hydrogen, alkyl, fluoro, chloro, carboxyl, alkoxy, alkyl carbonyl, aryl carbonyl, and amino;

30 and  $R^5$  and  $R^5$  are each independently selected from hydrogen, alkyl, alkoxy, fluoro, chloro, carboxy, alkyl carbonyl, aryl carbonyl, amino and together form a cyclic ring structure or a heterocyclic ring structure; and

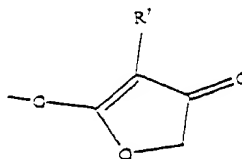
$R^6$  is selected from alkyl having 1 to 10 carbon atoms, aryl or substituted aryl;



wherein A is a covalently bonded amine protecting group, and  
n is 1-4, preferably 2;



15 where X is the pharmaceutically accepted salt, and  
n is 1-4, preferably 2; and



wherein  $R^7$  is selected from the group consisting of alkyl having 1 to 10 carbon atoms, aryl and alkylaryl or the pharmaceutically acceptable acid or base salts thereof; and a pharmaceutically acceptable excipient.

25 25. The pharmaceutical composition of Claim 24 wherein  $m = 2$ ,  $R^1$  and  $R^{1B}$  are each independently selected from methyl, ethyl, isopropyl and t-butyl.

26. The pharmaceutical composition of Claim 24 wherein  $m = 3$ ,  $R^1$ ,  $R^{1B}$  and  $R^{1C}$  are each independently selected from methyl, ethyl, isopropyl and t-butyl.

30 27. The pharmaceutical composition of Claim 25 wherein  $R^2$  is F or 2,6-difluorophenoxy,  $R^5$  and  $R^5$  are each hydrogen and  $R^6$  is methyl.

28. The pharmaceutical composition of Claim 26 wherein  $R^2$  is F or 2,6-difluorophenoxy,  $R^5$  and  $R^5$  are each hydrogen and  $R^6$  is methyl.

29. A method of treatment of a human being diagnosed as having arthritis, metastases, infectious diseases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerotitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease  
5 immune-based diseases, hypersensitivity, auto-immune diseases, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:

10 A. Administering a therapeutically effective amount of the pharmaceutical composition of Claim 2.

30. A method of treatment of a human being diagnosed as having arthritis, metastases, infectious diseases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerotitis, hepatitis, pancreatitis,  
15 reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, auto-immune diseases, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method  
20 comprises:

A. Administering a therapeutically effective amount of the pharmaceutical composition of Claim 9.

31. A method of treatment of a human being diagnosed as having arthritis, metastases, infectious diseases, meningitis, salpingitis, septic shock, respiratory diseases,  
25 inflammatory condition, cholangitis, colitis, encephalitis, endocerotitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, auto-immune diseases, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage,  
30 traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:

A. Administering a therapeutically effective amount of the pharmaceutical



composition of Claim 15.

32. A method of treatment of a human being diagnosed as having arthritis, metastases, infectious diseases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerotitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, auto-immune diseases, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method  
10 comprises:

A. Administering a therapeutically effective amount of the pharmaceutical composition of Claim 16.

33. A method of treatment of a human being diagnosed as having arthritis, metastases, infectious diseases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerotitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, auto-immune diseases, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method  
20 comprises:

A. Administering a therapeutically effective amount of the pharmaceutical composition of Claim 17.

34. A method of treatment of a human being diagnosed as having arthritis, metastases, infectious diseases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocerotitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, auto-immune diseases, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyltrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal chord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method  
30 comprises:

A. Administering a therapeutically effective amount of the pharmaceutical composition of Claim 24.

35. A method of treatment of a human being diagnosed as having arthritis, metastases, infectious diseases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocervicitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, auto-immune diseases, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyotrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal cord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:

A. Administering a therapeutically effective amount of the pharmaceutical composition of Claim 25.

36. A method of treatment of a human being diagnosed as having arthritis, metastases, infectious diseases, meningitis, salpingitis, septic shock, respiratory diseases, inflammatory condition, cholangitis, colitis, encephalitis, endocervicitis, hepatitis, pancreatitis, reperfusion injury, ischemic diseases, myocardial infarction, stroke, ischemic kidney disease immune-based diseases, hypersensitivity, auto-immune diseases, multiple sclerosis, bone diseases; and neurodegenerative diseases, Alzheimer's, Amyotrophic Lateral Sclerosis (ALS), Huntington's disease, Parkinson's disease, meningitis, spinal cord injuries and liver damage, traumatic brain injury, alopecia, AIDS and toxin induced liver disease, which method comprises:

A. Administering a therapeutically effective amount of the pharmaceutical composition of Claim 26.